

Sub-diffusion in External Potential: Anomalous hiding behind Normal

Sergei Fedotov, Nickolay Korabel

School of Mathematics, The University of Manchester, Manchester M13 9PL, UK

We propose a model of sub-diffusion in which an external force is acting on a particle at all times not only at the moment of jump. The implication of this assumption is the dependence of the random trapping time on the force with the dramatic change of particles behavior compared to the standard continuous time random walk model. Constant force leads to the transition from non-ergodic sub-diffusion to seemingly ergodic diffusive behavior. However, we show it remains anomalous in a sense that the diffusion coefficient depends on the force and the anomalous exponent. For the quadratic potential we find that the anomalous exponent defines not only the speed of convergence but also the stationary distribution which is different from standard Boltzmann equilibrium.

PACS numbers: 02.50.-r, 05.40.Fb, 05.10.Gg, 45.10.Hj

Recently it has become clear that anomalous diffusion measured by a non-linear growth of the ensemble averaged mean squared displacement $\langle x^2 \rangle \sim t^\mu$ with the anomalous exponent $\mu \neq 1$ is as widespread and important as normal diffusion with $\mu = 1$ [1]. Sub-diffusion with $\mu < 1$ was observed in many physical and biological systems such as porous media [2], glass-forming systems [3], motion of single viruses in the cell [4], cell membranes [5, 6], and inside living cells [7–9]. Many examples of sub-diffusive processes in biological systems can be found in recent reviews [10, 11]. Nowadays new tools are available including super-resolution light optical microscopy techniques to deal with biological in vivo data which allows to monitor a large number of trajectories at the single-molecule level and at nanometer resolution [12–14]. Using these techniques it is possible to discriminate between anomalous ergodic processes where the ensemble and time averages coincide and non-ergodic processes where ensemble and time averages have different behavior [15–17]. Two important observations have been made about anomalous transport in living cells: (1) anomalous transport is usually a transient phenomenon before transition to normal diffusion or saturation due to confined space [18–20] (2) ergodic and non-ergodic processes may coexist as it was observed in plasma membrane [21].

Several models are proposed to describe ergodic and non-ergodic anomalous processes such as non-ergodic continuous time random walk (CTRW) with power-law tail waiting times, ergodic anomalous process generated by fractal structures, fractional Brownian-Langevin motion characterized by long correlations and time dependent diffusion coefficient [1, 22, 23]. The standard CTRW model for sub-diffusion of a particle in an external field $F(x)$ randomly moving along discrete one-dimensional lattice can be described by the generalized master equation for the probability density $p(x, t)$ to find the particle at position x at time t

$$\frac{\partial p}{\partial t} = -i(x, t) + w^+(x-a)i(x-a, t) + w^-(x+a)i(x+a, t), \quad (1)$$

where a is the lattice spacing and $i(x, t)$ is the total escape

rate from x

$$i(x, t) = \frac{1}{\Gamma(1-\mu)\tau_0^\mu} \mathcal{D}_t^{1-\mu} p(x, t). \quad (2)$$

Here τ_0 is a constant timescale and $\mathcal{D}_t^{1-\mu}$ is the Riemann-Liouville fractional derivative defined by

$$\mathcal{D}_t^{1-\mu} p(x, t) = \frac{1}{\Gamma(\mu)} \frac{\partial}{\partial t} \int_0^t \frac{p(x, \tau)}{(t-\tau)^{1-\mu}} d\tau. \quad (3)$$

The probabilities of jumping to the right $w^+(x)$ and to the left $w^-(x)$ are

$$w^+(x) = \frac{1}{2} + \beta a F(x), \quad w^-(x) = \frac{1}{2} - \beta a F(x). \quad (4)$$

Series expansion of Eq. (1) together with Eq. (2) and Eq. (4) leads to the fractional Fokker-Planck equation (FFPE) [24, 25]

$$\frac{\partial p}{\partial t} = D_\mu \left[\frac{\partial^2}{\partial x^2} - \beta \frac{\partial}{\partial x} F(x) \right] \mathcal{D}_t^{1-\mu} p, \quad (5)$$

where the generalized diffusion $D_\mu = a^2/(2\Gamma(1-\mu)\tau_0^\mu)$. The stationary solution of Eq. (5) is the Boltzmann distribution. There exist a huge literature on this equation [24, 25] and its generalization for time dependent forces [26–32].

One of the main assumptions in this literature, which is not always clearly stated is that, as long as a random walker is trapped at a particular point x , the external force $F(x)$ does not influence the particle. It is clear from Eq. (2) that the escape rate $i(x, t)$ does not depend on the external force $F(x)$. The force only acts at the moment of escape inducing a bias. The question is how to take into account the dependence of the escape rate on $F(x)$? To the author's knowledge this is still an open question. One of the main aims of this Letter is to propose a model which deals with this problem. We find that the dependence of escape rate on force drastically changes the form of the master equation (1) and FFPE (5). We observe transient anomalous diffusion and transition from non-ergodic to normal ergodic behavior. However, we show

that this seemingly normal process could be still anomalous masked by normal behavior. Our findings suggest that a closer inspection of experimental results could be necessary in order to discriminate between normal and anomalous processes.

Model. — We consider a random particle moving on a one dimensional lattice under assumption that an external force acts on a particle at all times not only at the moment of jump as in Eq. (1). The implication of this assumption is the dependence of the random trapping time on the external force (not just jumping probabilities as in (4)). Some discussion of situation when the external force influence the rates and jumps can be found in [26]. The main physical idea behind our model is that there exists two independent mechanism of escaping from the point x with two different random residence times. The first mechanism is due to external force with the escape rate proportional to $F(x)$. The second one is the sub-diffusive mechanism involving the rate inversely proportional to the residence time. The latter generates the power law waiting time distribution with the infinite first moment.

Regarding the first mechanism, we define the jump process from the point x as follows. We assume that the rate of jump to the right \mathbb{T}_x^+ from x to $x+a$ is $\nu a F(x)$ when $F(x) \geq 0$ and the rate of jump to the left \mathbb{T}_x^- from x to $x-a$ is $-\nu a F(x)$ when $F(x) \leq 0$. For this jump model the random waiting time T_F at the point x is defined by the exponential survival probability $\Psi_F(x, \tau)$ involving the external force $F(x)$

$$\Psi_F(x, \tau) = \Pr\{T_F > \tau\} = \exp(-\nu a |F(x)| \tau). \quad (6)$$

where ν is the intensity of jumps due to force field. For example, one can think of the escape rate \mathbb{T}_x^+ that is defined in terms of the potential field $U(x)$ that is $\mathbb{T}_x^+ = -\nu [U(x+a) - U(x)] > 0$, there $F(x) = -U'(x) + o(a^2)$ for $U'(x) \leq 0$. The second mechanism involves the sub-diffusive random walk with the escape rate $\lambda(x, \tau)$ from the point x , which is inversely proportional to the residence time τ . In this case the random waiting time T_λ at the point x is defined by the survival probability

$$\Psi_\lambda(x, \tau) = \Pr\{T_\lambda > \tau\} = \exp\left(-\int_0^\tau \lambda(x, s) ds\right). \quad (7)$$

The question now is how to implement the jumping process due to external force into the sub-diffusive random walk scheme? When the random walker makes a jump to the point x , it spends some random time (residence time) before making another jump to $x+a$ or $x-a$. Let us denote this residence time T_x . The key point of our model is that we define this residence time as the minimum of two: T_λ and T_F

$$T_x = \min(T_\lambda, T_F). \quad (8)$$

For the anomalous sub-diffusive case this model could lead to the drastic change in the form of the fractional master equation. The main reason for this is that the external force $F(x)$ plays the role of tempering factor preventing the random walker to be anomalously trapped

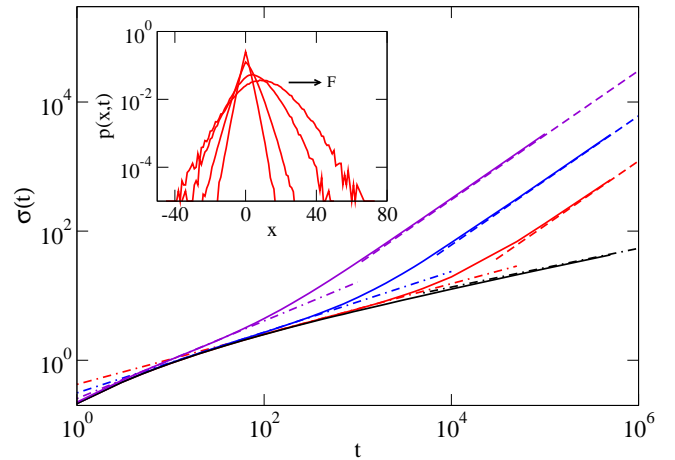


FIG. 1: Variance $\sigma(t)$ of ensemble calculated with $\mu = 0.3$ and $p(x, 0) = \delta(x)$. In all simulations we use $\nu = 1$. For $F = 0$ (lowest curve) the variance grows as $D_\mu t^\mu$ (dashed-dotted line) in the limit $t \rightarrow \infty$. Constant force $F = 0.0001$, $F = 0.001$ and $F = 0.01$ (curves from bottom to top on the RHS of the figure) leads to the transition from sub-diffusive behavior for short times to normal diffusion in the long time limit, $\sigma \rightarrow 2D_F t$ (dashed lines), with D_F given by Eq. (13). Intermediate asymptotic of the variance is fitted by the power law (dashed-dotted lines, see the text). The inset shows transition of densities from sub-diffusive form for short times to the Gaussian shape for long times caused by the constant force $F = 0.0001$. Densities were calculated at $t = 10^3, 10^4, 5 \cdot 10^4$ and 10^5 .

at point x . Because of the independence of two mechanisms, in our model the rate of jump \mathbb{T}_x^+ to the right from x to $x+a$ and the rate of jump \mathbb{T}_x^- to the left from x to $x-a$ can be written as the sum

$$\mathbb{T}_x^+ = \begin{cases} \omega^+(x) \lambda(x, \tau) + \nu a F(x), & F(x) \geq 0, \\ \omega^-(x) \lambda(x, \tau), & F(x) < 0 \end{cases} \quad (9)$$

and

$$\mathbb{T}_x^- = \begin{cases} \omega^+(x) \lambda(x, \tau), & F(x) \geq 0, \\ \omega^-(x) \lambda(x, \tau) - \nu a F(x), & F(x) < 0. \end{cases} \quad (10)$$

Although it is straightforward to consider general $\omega^+(x)$, $\omega^-(x)$, for simplicity in what follows we consider $\omega^+(x) = \omega^-(x) = 1/2$. In our model the asymmetry of random walk occur only from the force dependent rate. Let us explain the main idea of Eqs. (9) and (10). The external force $F(x) \geq 0$ increases the sub-diffusive rate of jumps to the right $\lambda(x, \tau)/2$ and does not change the sub-diffusive rate of jumps to the left. The essential property of Eqs. (9) and (10) is that the rate $\lambda(x, \tau)$ depends on the residence time variable τ . This dependence makes any model involving the probability density $p(x, t)$ non-Markovian. For the Markov case with $F(x) = 0$, $\lambda^{-1}(x)$ has a meaning of the mean residence time at the point x . When the parameter $\nu = 0$ and the rates are $\mathbb{T}_x^+ = \omega^+(x) \lambda(x, \tau)$, $\mathbb{T}_x^- = \omega^-(x) \lambda(x, \tau)$, we obtain the standard fractional

Fokker-Planck equation (5). Notice that Eq. (8) is consistent with the expression for the effective escape rate $\mathbb{T}_x^+ + \mathbb{T}_x^-$ as a sum of two rates $\lambda(x, \tau) + \nu a |F(x)|$. Similar situation has been considered in [40].

After incorporation of the force dependent escape rates we can obtain generalized master equation (see Supplementary Materials for the derivation). By expanding the RHS of the master equation to the second order in jump size a , we get a fractional diffusion equation

$$\frac{\partial p}{\partial t} = \frac{\partial^2}{\partial x^2} \left[D_\mu e^{-\nu a |F(x)|t} \mathcal{D}_t^{1-\mu} \left[p(x, t) e^{\nu a |F(x)|t} \right] \right] - a^2 \nu \frac{\partial}{\partial x} [F(x) p(x, t)]. \quad (11)$$

This equation is fundamentally different from the classical FFPE (5) because it involves the external force in both terms on the right hand side. One can see that the force $F(x)$ not only determines the advection term as in Eq. (5), but also plays the role of tempering parameter through the factor $e^{\nu a |F(x)|t}$. Similar factor occurs in sub-diffusive equation with the death or evanescent process [34, 35]. However, here we consider the system with constant total number of particle.

The stationary solution $p_{st}(x)$ of Eq. (11) obeys the standard equation

$$-a^2 \nu F(x) p_{st}(x) + \frac{d}{dx} [D_F(x) p_{st}(x)] = 0. \quad (12)$$

(see a supplement material for details). Interesting property of this equation is that the effective diffusion constant $D_F(x)$ depends on the external force and anomalous exponent

$$D_F(x) = D_\mu (\nu a |F(x)|)^{1-\mu}. \quad (13)$$

This fact implies that the Boltzmann distribution is no longer stationary solution of (12). For the quadratic potential $U(x) = \kappa x^2/2$ with $F(x) = kx$, we find that for large x the stationary density $p_{st}(x)$ has the form

$$p_{st}(x) \sim \exp(-A|x|^{1+\mu}), \quad (14)$$

where $A > 0$ is a constant. One can see that the form of stationary density is determined by the anomalous exponent μ . In this case the particles spread further compared to the Boltzmann case. The reason is the dependence of the effective diffusion constant $D_F(x)$ on force $F(x)$. Note that for the sub-diffusive fractional Fokker-Planck equation (5) the anomalous exponent only determines the slow power law relaxation rate, while the stationary density converges to Boltzmann equilibrium which does not depend on μ .

Numerical simulations.— We consider two particular cases: (1) constant force F corresponding to the linear potential and (2) the quadratic potential $U(x) = \kappa x^2/2$ both in the infinite domain. We concentrate on

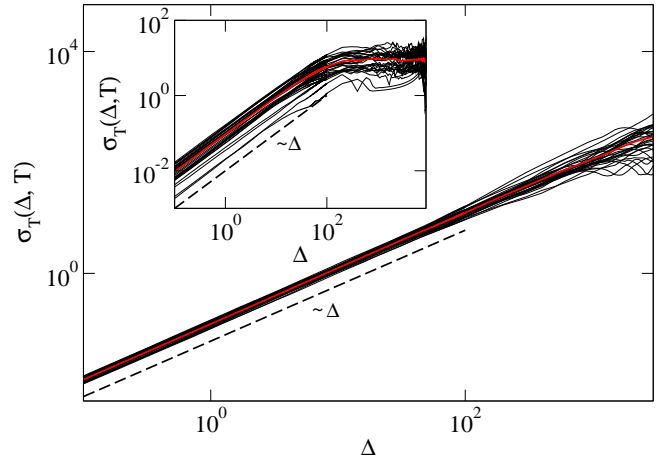


FIG. 2: Time averaged variance $\sigma_T(\Delta, T)$ calculated for 30 individual trajectories of the length $t = 10^4$ (each curve corresponds to a single trajectory) with $\mu = 0.7$. The minor scatter between trajectories reflects the ergodic behavior under the action of constant external force (main figure). Contrast this with the behavior of the time averaged variance in quadratic potential (the inset). The scatter between individual trajectories indicates that the system is non-ergodic in this case. The red (bold solid) lines represent average over 30 trajectories.

the behavior of the density function $p(x, t)$, the mean $\langle x(t) \rangle$ and the variance $\sigma(t) = \langle x^2 \rangle - \langle x \rangle^2$ calculated using an ensemble of trajectories from the initial distribution $p(x, 0) = \delta(x)$. We also calculate the time averaged variance of a single trajectory of length T , $\sigma_T(\Delta, T) = \delta^2(\Delta, T) - (\delta(\Delta, T))^2$, where $\delta^n(\Delta, T) = \int_0^{T-\Delta} (x(t+\Delta) - x(t))^n dt / (T - \Delta)$, $n = 1, 2$. This quantity become a standard tool to assess ergodic properties of a system been equivalent to its ensemble averaged counterpart only for ergodic case.

When the external force F is constant, we observe the transition from sub-diffusion at short times to seemingly normal diffusion at long times. The density function changes from the distinct sub-diffusive shape for short times to the Gaussian shape propagator at longer times (see the inset of figure 1). The average position of the ensemble behaves as $\langle x(t) \rangle = Ft$. The ensemble averaged variance $\sigma(t)$ grows as a power law for short times, $\sigma(t) \sim t^\eta$, and transition to a normal diffusive linear growth $\sigma(t) \sim 2D_F t$ for longer times. However, in this case the diffusion coefficient D_F depends on the force F and anomalous exponent μ . We conclude that although the variance $\sigma(t)$ is linearly proportional to time, this dependence reveals the anomalous nature of the process even in the limit $t \rightarrow \infty$. Numerical calculations confirms the analytical result for the diffusion coefficient Eq. (13) (see figure 1). Second observation is that the power law behavior at short times involves the exponent $\eta(F) > \mu$ which depends on force F . For $\mu = 0.3$ they are estimated to be $\eta \approx 0.39$ for $F = 0.0001$, $\eta \approx 0.47$ for $F = 0.001$ and $\eta \approx 0.6$ for $F = 0.01$. This can be interpreted as an enhancement of sub-diffusion caused by the

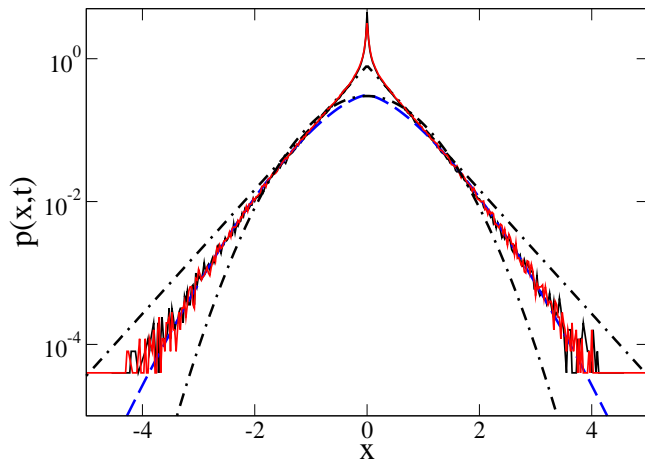


FIG. 3: Density $p(x, t)$ in the quadratic potential $U(x) = kx^2$, $k = 0.001$ calculated with the anomalous exponent $\mu = 0.5$ at time $t = 10^5$ and $t = 10^6$. Two densities overlap indicating convergence to stationary solution p_{st} . Clearly p_{st} is non-Boltzmann and is well described (accept for the central part) by the long-wave asymptotic Eq. (12) shown by the dashed line. To distinguish the form of the stationary solution $\exp(-A|x|^{1+\mu})$, we show the Boltzmann equilibrium $\exp(-Bx^2)$ and the function $\exp(-C|x|)$ (dashed-dotted curves) to guide the eye (A, B, C are positive constants). Note that the central part of p_{st} has distinct cusp at $x = 0$ where the force vanishes.

constant force. Such enhancement should be taken into account in the analysis of biological experiments where sub-diffusion usually appears as transient before the transition to the normal diffusion [10]. For the large value of F the exponent η tends to one while in the small force limit $\eta \rightarrow \mu$. The time averaged variance calculated for constant force grows linearly $\sigma_T(\Delta, T) \sim \Delta$ and shows minor scatter between single trajectories (figure 2). After averaging over different trajectories, it grows with the coefficient $2D_F$ which is equal to the ensemble average value. This shows that the non-ergodic sub-diffusive system becomes an ergodic one.

Now we consider the quadratic potential $U(x) = \kappa x^2/2$. The system becomes again non-ergodic despite the tempering affect of the force. To confirm this we calculate the time averaged variance (inset of figure 2). As expected it shows large fluctuations among different trajectories typical for non-ergodic systems. Note that even with this typical behavior, it can be easily distinguished in experiments since in our case the mean of the time averaged variance converges to a constant, while for standard CTRW in a bounded region it grows as a power

of the anomalous exponent, $\langle \sigma_T(\Delta) \rangle \sim \Delta^{1-\mu}$. Regarding the shape of the stationary density, numerical simulations are in good agreement with analytical results Eq. (14) (see figure 3).

Summary.— In this Letter we have presented a model of anomalous sub-diffusive transport in which the force acts on the particle at all times not only at the moment of jump. This leads to the dependence of jumping rate on the force with the dramatic change of particles behavior compared to the standard CTRW model. We have derived a new type of fractional diffusion equation which is fundamentally different from the classical fractional Fokker-Planck equation. In our model the force $F(x)$ not only appears in the drift term as in Eq. (5), but also determines the structure of the diffusion term controlling the spread of particles. The constant external force leads to the natural tempering of the broad waiting time distribution and, as a result, to the transition to a seemingly normal diffusion (linear growth of the mean squared displacement) and equivalence of the time and ensemble averages. However, this may lead to a wrong conclusion in analyzes of experimental results on transient sub-diffusion [10] that the process is normal for large times. We have found that contrary to normal diffusion process in the external force field, the diffusion coefficient depends on the force and anomalous exponent. This fact implies that the Boltzmann distribution is no longer stationary solution. External perturbations and noise fluctuations are not separable which reflects the non-Markovian nature of the process even for large times.

Our results would be possible to test in experiments, for example, by considering a bead which is moving sub-diffusively in an actin network. The motion of such a beat can be described by a random walk type of dynamics [37]. Force-measurements could be realized by using optical trap and tweezers which are the nano-tools capable of performing such measurements on individual molecules and organelles within the living cell [14]. When the force is constant the dependence of the measures diffusion coefficient on the strength of the force would reveal the predicted power law behavior $F^{1-\mu}$. For quadratic potential it could be possible to retrieve the form of the stationary profile (14) with the slow decay compared to Boltzmann distribution for large x .

Acknowledgements

SF and NK acknowledge the support of the EPSRC Grant EP/J019526/1.

-
- [1] *Anomalous Transport: Foundations and Applications*, edited by R. Klages, G. Radons, and I.M. Sokolov (Wiley-VCH, Weinheim, 2007).
 - [2] G. Drazer and D.H. Zanette, Phys. Rev. E **60**, 5858

- (1999).
- [3] E.R. Weeks and D.A. Weitz, Chem. Phys. **284**, 361 (2002).
- [4] G. Seisenberger *et al.*, Science **294**, 1929 (2001).

- [5] M.J. Saxton and K. Jacobson, Ann. Rev. Biophys. Biomol. Struct. **26**, 373 (1997).
- [6] K. Ritchie *et al.*, Biophys. J. **88**, 2266 (2005).
- [7] M. Weiss, H. Hashimoto, and T. Nilsson, Biophys. J. **84**, 4043 (2003).
- [8] I. Golding and E.C. Cox, Phys. Rev. Lett. **96**, 098102 (2006).
- [9] I.M. Tolic-Norrelykke *et al.*, Phys. Rev. Lett. **93**, 078102 (2004).
- [10] F. Höfling and T. Franosch, Rep. Prog. Phys. **76**, 046602 (2013).
- [11] E. Barkai, Y. Garini, and R. Metzler, Phys. Today **65** 29 (2012).
- [12] A. Sergé *et al.*, Nat. Methods **5**, 687 (2008).
- [13] K. Jaqaman *et al.*, Nat. Methods **5**, 695 (2008).
- [14] K. Norregaard *et al.*, Phys. Chem. Chem. Phys. **16**, 12614 (2014).
- [15] Y. He *et al.*, Phys. Rev. Lett. **101**, 058101 (2008).
- [16] A. Lubelski, I.M. Sokolov, and J. Klafter, Phys. Rev. Lett. **100**, 250602 (2008).
- [17] Y. Meroz, I.M. Sokolov and J. Klafter, Phys. Rev. Lett. **110**, 090601 (2013).
- [18] I. Bronstein *et al.*, Phys. Rev. Lett. **103**, 018102 (2009).
- [19] T. Neusius *et al.*, Phys. Rev. Lett. **100**, 188103 (2008).
- [20] M. Saxton, Biophys. J. **81**, 2226 (2001).
- [21] A.V. Weigel *et al.*, Proc. Natl. Acad. Sci. USA **108**, 6438 (2011).
- [22] I.M. Sokolov, Soft Matter **8**, 9043 (2012).
- [23] P.C. Bressloff and J.M. Newby, Rev. Mod. Phys. **85**, 135 (2013).
- [24] R. Metzler, E. Barkai, and J. Klafter, Phys. Rev. Lett. **82**, 3563 (1999).
- [25] R. Metzler and J. Klafter, Phys. Reports **339**, 1 (2000).
- [26] E. Heinsalu *et al.*, Phys. Rev. Lett. **99**, 120602 (2007).
- [27] M. Magdziarz, A. Weron, and J. Klafter, Phys. Rev. Lett. **101**, 210601 (2008).
- [28] B.I. Henry, T.A.M. Langlands, and P. Straka, Phys. Rev. Lett. **105**, 170602 (2010).
- [29] S. Eule and R. Friedrich, Euro. Phys. Lett. **86**, 30008 (2009).
- [30] I.M. Sokolov and J. Klafter, Phys. Rev. Lett. **97**, 140602 (2006).
- [31] A.I. Shushin, Phys. Rev. E **78**, 051121 (2008).
- [32] V.P. Shkilev, Journal of Experimental and Theoretical Physics, **114**, 830 (2012).
- [33] S. Fedotov, A.O. Ivanov and A.Y. Zubarev, Math. Model. Nat. Phenom. **8**, 28 (2013).
- [34] E. Abad, S.B. Yuste, and K. Lindenberg, Phys. Rev. E **81**, 031115 (2010).
- [35] S. Fedotov and S. Falconer, Phys. Rev. E **87**, 052139 (2013).
- [36] T. Neusius, I.M. Sokolov and J.C. Smith, Phys. Rev. E **80**, 011109 (2009).
- [37] I.Y. Wong *et al.*, Phys. Rev. Lett. **92**, 178101 (2004).
- [38] D.R. Cox and H.D. Miller, *The Theory of Stochastic Processes* (Methuen, London, 1965).
- [39] A.V. Chechkin, R. Gorenflo, and I.M. Sokolov, J. Phys. A: Math. Gen. **38**, L679 (2005).
- [40] S. Fedotov, Phys. Rev. E **88**, 032104 (2013).

SUPPLEMENTARY MATERIALS

To derive Eq. (11) we use the structured probability density function $\xi(x, t, \tau)$ with the residence time τ as auxiliary variable. This density gives the probability that the particle position $X(t)$ at time t is at the point x and its random residence time T_x at point x is in the interval $(\tau, \tau + d\tau)$. The density $\xi(x, t, \tau)$ obeys the balance equation

$$\frac{\partial \xi}{\partial t} + \frac{\partial \xi}{\partial \tau} = -(\mathbb{T}_x^+(x, \tau) + \mathbb{T}_x^-(x, \tau)) \xi. \quad (15)$$

We consider only the case when the residence time of random walker at $t = 0$ is equal to zero, so the initial condition is

$$\xi(x, 0, \tau) = p_0(x) \delta(\tau), \quad (16)$$

where $p_0(x)$ is the initial density. The boundary condition in terms of residence time variable ($\tau = 0$) can be written as [38]

$$\begin{aligned} \xi(x, t, 0) = & \int_0^t \mathbb{T}_x^+(x - a, \tau) \xi(x - a, t, \tau) d\tau + \\ & \int_0^t \mathbb{T}_x^-(x + a, \tau) \xi(x + a, t, \tau) d\tau. \end{aligned} \quad (17)$$

We solve (15) by the method of characteristics for $\tau < t$

$$\xi(x, t, \tau) = j(x, t - \tau) \Psi_\lambda(x, \tau) e^{-\Phi(x)\tau}, \quad \tau < t, \quad (18)$$

where

$$\Phi(x) = \nu a |F(x)|. \quad (19)$$

The solution Eq. (18) is written in terms of the integral arrival rate $j(x, t) = \xi(x, t, 0)$ and in terms of the survival function Eq. (7)

$$\Psi_\lambda(x, \tau) = e^{-\int_0^\tau \lambda(x, s) ds}. \quad (20)$$

Our purpose now is to derive the master equation for the probability density

$$p(x, t) = \int_0^{t^+} \xi(x, t, \tau) d\tau. \quad (21)$$

Let us introduce the integral escape rate to the right $i^+(x, t)$ and the integral escape rate to the left $i^-(x, t)$ as

$$i^\pm(x, t) = \int_0^{t^+} \omega^\pm(x) \lambda(x, \tau) \xi(x, t, \tau) d\tau. \quad (22)$$

Note that the integration with respect to the residence time τ in (21) and (22) involves the upper limit $\tau = t$, where we have a singularity due to the initial condition (16). Then the boundary conditions (17) can be written in a simple form:

$$\begin{aligned} j(x, t) = & i^+(x - a, t) + i^-(x + a, t) \\ & + \begin{cases} \nu a F(x - a) p(x - a, t), & F \geq 0 \\ -\nu a F(x + a) p(x + a, t), & F < 0. \end{cases} \end{aligned} \quad (23)$$

It follows from (16), (18) and (22) that

$$i^\pm(x, t) = \int_0^t \psi^\pm(x, \tau) j(x, t - \tau) e^{-\Phi(x)\tau} d\tau + \psi^\pm(x, t) p_0(x) e^{-\Phi(x)t}, \quad (24)$$

where $\psi^+(x, \tau) = \omega^+(x) \lambda(x, \tau) \Psi_\lambda(x, \tau)$ and $\psi^-(x, \tau) = \omega^-(x) \lambda(x, \tau) \Psi_\lambda(x, \tau)$. Substitution of (16) and (18) to (21), gives

$$p(x, t) = \int_0^t \Psi_\lambda(x, \tau) j(x, t - \tau) e^{-\Phi(x)\tau} d\tau + \Psi_\lambda(x, t) p_0(x) e^{-\Phi(x)t}. \quad (25)$$

The balance equation for probability density $p(x, t)$ can be written as

$$\frac{\partial p}{\partial t} = -i^+(x, t) - i^-(x, t) + j(x, t) - \Phi(x)p(x, t). \quad (26)$$

Let us find a closed equation for $p(x, t)$ by expressing integral rates $i^\pm(x, t)$ and $j(x, t)$ in terms of the density $p(x, t)$. We apply the Laplace transform $\hat{f}(s) = \int_0^\infty f(\tau) e^{-s\tau} d\tau$ to (24), and (25), and obtain

$$\hat{i}^\pm(x, s) = \frac{\hat{\psi}^\pm(x, s + \Phi(x))}{\hat{\Psi}(x, s + \Phi(x))} \hat{p}(x, s), \quad (27)$$

which after the inversion of the Laplace transform and using the shift theorem gives

$$i^\pm(x, t) = \int_0^t K^\pm(x, t - \tau) e^{-\Phi(x)(t-\tau)} p(x, \tau) d\tau. \quad (28)$$

The memory kernels $K^+(x, t)$ and $K^-(x, t)$ are defined by Laplace transforms

$$\hat{K}^\pm(x, s) = \hat{\psi}^\pm(x, s) / \hat{\Psi}_\lambda(x, s). \quad (29)$$

Now we consider the sub-diffusive case where $\lambda(\tau)$ is inversely proportional to the residence time τ :

$$\lambda(\tau) = \mu / (\tau_0 + \tau), \quad 0 < \mu < 1. \quad (30)$$

For simplicity we consider

$$\omega^- = \omega^+ = 1/2. \quad (31)$$

It is straightforward to generalize to non-homogeneous systems by considering space dependent $\lambda(x)$ and space dependent anomalous exponent $\mu(x)$, this case we consider elsewhere [39, 40]. From Eqs. (7) and (30) it follows that the survival function has a power-law dependence

$$\Psi_\lambda(\tau) = \tau_0^\mu (\tau_0 + \tau)^{-\mu}. \quad (32)$$

The waiting time density functions $\psi^\pm(\tau)$ are

$$\psi^+(\tau) = \psi^-(\tau) = \mu \tau_0^\mu (\tau_0 + \tau)^{-1-\mu} / 2. \quad (33)$$

Using the Tauberian theorem their Laplace transforms are $\hat{\psi}^\pm(s) \simeq (1 - gs^\mu)/2$ as $s \rightarrow 0$, where $g = \Gamma(1 - \mu) \tau_0^\mu$. From (29) we obtain the Laplace transforms

$$\hat{K}^+(s) = \hat{K}^-(s) \simeq s^{1-\mu} / (2g), \quad s \rightarrow 0. \quad (34)$$

Therefore, the integral escape rates to the right i^+ and to the left i^- in the sub-diffusive case are

$$i^+(x, t) = i^-(x, t) = e^{-\Phi(x)t} \mathcal{D}_t^{1-\mu} [p(x, t) e^{\Phi(x)t}] / (2g). \quad (35)$$

By introducing the total integral escape rate

$$i(x, t) = i^+(x, t) + i^-(x, t), \quad (36)$$

and expanding the right-hand side of Eq. (26) to second order in jump size a we obtain the following fractional equation

$$\frac{\partial p}{\partial t} = -a^2 \nu \frac{\partial}{\partial x} [F(x)p(x, t)] + \frac{a^2}{2} \frac{\partial^2 i}{\partial x^2}, \quad (37)$$

which using Eq. (35) leads to the main equation of the paper Eq. (11).

Now we derive the equation for the stationary solution Eq. (12). Writing the escape rate $i(x, t)$ in Laplace form

$$\hat{i}(x, s) = \frac{(s + \Phi(x))^{1-\mu}}{g} \hat{p}(x, s) \quad (38)$$

and taking the limit $s \rightarrow 0$ corresponding to $t \rightarrow \infty$, we obtain the stationary escape rate

$$i_{st}(x) = \frac{\Phi(x)^{1-\mu}}{g} p_{st}(x). \quad (39)$$

where the stationary density is defined in a standard way $p_{st}(x) = \lim_{s \rightarrow 0} s \hat{p}(x, s)$. Taking the time derivative in Eq. (37) to zero and substituting Eq. (39) we obtain the stationary advection-diffusion equation

$$-a^2 \nu \frac{d}{dx} [F(x)p_{st}(x)] + \frac{d^2}{dx^2} [D_F(x)p_{st}(x)] = 0. \quad (40)$$

Integrating Eq. (40) and taking into account that the flux of the particles is zero we obtain Eq. (12).